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(54) Abstract Title
Preparation of 2-Mercaptothiazole

(57) A process for preparing 2-mercaptothiazole by reacting a water soluble salt of dithiocarbamic acid with 2-haloacetaldehyde characterised in that either the 2-haloacetaldehyde is added to a slum of the salt of dithiocarbamic acid in solid form in a water-miscible diluent in which the salt is substantially insoluble, or the 2-haloacetaldehyde and a solution of the the salt of dithiocarbamic acid are separately and simultaneously delivered at substantially equimolar rates of addition to a reaction vessel containing a water-miscible diluent in which the salt is substantially insoluble.

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PROCESS FOR PREPARATION OF HETEROCYCLIC THIOL

This invention relates to an improved process for preparing 2-mercaptothiazole.

The preparation of 2-mercaptothiazole (also known as 2-thiazolethiol and, in its tautomer form, as (3H)-2-thiazolethione) by the reaction of 2-chloroacetaldehyde with ammonium dithiocarbamate is described in US patent 2426397 and by Mathes R A, *et al*, *J Amer Chem Soc*, 70, 1451-2 (1948). The process involves addition of an ethanolic solution of 2-chloroacetaldehyde to an aqueous solution of ammonium dithiocarbamate. The authors state that they were unable to increase the yield of 50% based on chloroacetaldehyde by varying the reaction conditions, such as by reversing the order or length of time of addition, the reaction temperature, concentration of reactants, pH control and use of organic solvents as reaction diluents. In addition the authors report that the process was accompanied by troublesome side reactions giving rise to gummy by-products. Surprisingly there has been no subsequently reported studies aimed at improving the yield of product from this reaction.

The present invention concerns an improved process for the preparation of 2-mercaptothiazole based upon the reaction of 2-haloacetaldehydes with salts of dithiocarbamic acid in which substantially improved yields of the product may be obtained as compared with the prior art process referred to above, and without the concommitant production of gummy materials.

Accordingly there is provided a process for the preparation of 2-mercaptothiazole by reacting a water soluble salt of dithiocarbamic acid with 2-haloacetaldehyde characterised in that the 2-haloacetaldehyde is added to a slurry of the salt of dithiocarbamic acid in solid form in a water-miscible diluent in which the salt is substantially insoluble. By slurry is meant a mobile mixture of the salt, in powdered or granular form, with the diluent.

In a preferred form of the process the slurry is maintained at a temperature within the range -10°C to +15°C during the addition. This is conveniently at or below 0°C and can, for example, be achieved by circulating iced water or cooled brine through a cooling bath or jacket surrounding the reaction vessel. The reaction itself is exothermic and it is therefore preferable to control the rate of addition of the 2-haloacetaldehyde so as to maintain the temperature within the preferred range until the addition has been completed. It is usual to

agitate of stir the contents of the reaction vessel during the addition to facilitate mixing and to prevent the build up of local concentrations of the added material.

In a variant of the above process the 2-haloacetaldehyde and the solution of the salt of dithiocarbamic acid are separately and simultaneously delivered at substantially equimolar rates of addition to a reaction vessel containing a water-miscible diluent in which the salt is substantially insoluble. Preferably the diluent is primed with a minor amount of the solution of the salt of dithiocarbamic acid prior to the addition of the 2-haloacetaldehyde.

The 2-haloacetaldehyde is conveniently added in the form of an aqueous solution, and preferably on containing from 30 to 65% w/v of the 2-haloacetaldehyde, which can be present in the form of the hydrate. An aqueous solution is one in which the solvent is water or mainly water, the balance being water miscible organic solvents which do not interfere with the process such as lower alcohols, eg methanol or ethanol. Preferred 2-haloacetaldehydes for use in the invention process are 2-bromoacetaldehyde and 2-chloroacetaldehyde. An aqueous solution containing about 50% w/v of 2-chloroacetaldehyde hydrate is particularly preferred.

The water soluble salt of dithiocarbamic acid may be the ammonium salt, a quaternary ammonium salt or an alkali metal salt, such as the potassium salt or the sodium salt. However any water soluble salt with a non-interfering cationic species may be used. The ammonium salt is particularly preferred because of its easy preparation by the reaction of carbon disulfide with ammonia. It may be obtained in a solid form by conducting the reaction in an organic diluent in which ammonium dithiocarbamate is insoluble, for example an aliphatic hydrocarbon such as hexane, an ether such as tetrahydrofuran, or an aromatic hydrocarbon such as toluene.

In an alternative procedure the alkali metal salt, such as the sodium or potassium salt, of the dithiocarbamic acid may be used. A particularly convenient method for preparing the alkali metal salt is by reaction of a tertiary ammonium salt of dithiocarbamic acid with an alkali metal hydroxide. The tertiary ammonium salt can be obtained by reacting carbon disulfide with ammonia in the presence of a molar equivalent or more of the tertiary amine having a pK_b greater than that of ammonia under the reaction conditions. A tertiary amine which is substantially immiscible in water is preferred, such as a trialkylamine having at least 8 carbon atoms, for example triisopropylammine or ethyldiisopropylamine which is also

known as Hunig's base. The tertiary amine released by the reaction with the alkali metal hydroxide separates out from the reaction mixture and may be recovered any used to prepare more of the tertiary ammonium salt.

The water soluble salt of dithiocarbamic acid is suspended in a liquid diluent to form a slurry. The diluent may be selected from those in which the salt is substantially insoluble, and preferably has less that 1% solubility at 25°C, and which is miscible with water. Lower alkanols containing from 1 to 4 carbon atoms are particularly preferred, such as ethanol, n- and isopropanol and t-butanol. In order for the reaction to proceed efficiently the slurry must be mobile when agitated or stirred, and the ratio of the salt to diluent is preferably in the range 1:1.5 to 1:6 (w/v).

After the addition of the 2-haloacetaldehyde the reaction mixture may be heated at a temperature within the range 50°C to the reflux temperature to drive the reaction to completion. A preferred temperature is within the range 50°C to 75°C. The progress of the reaction can be monitored by withdrawing samples from time to time and subjecting them to analysis, for example, by HPLC. The period of heating to complete the reaction will depend upon such factors as the temperature, the concentration of the reactants and the amount and type of agitation of stirring, but usually a period of 5 to 24 hours will be sufficient.

However the period of heating may be significantly reduced if the pH of the reaction mixture is adjusted after the addition of the 2-haloacetaldehyde to a value within the range 1 to 3 by addition of a pH adjusting amount of an acidic substance, such as a concentrated mineral acid, for example hydrochloric acid or sulfuric acid. When the pH is adjusted in this way the period of heating can be reduced to 2 hours or less.

At the conclusion of the period of heating the desired product can be recovered from the reaction mixture by conventional procedures. Thus the mixture can be allowed to cool and the insolubles removed after which the more volatile solvents and diluents can be removed by evaporation. The residual mixture can then be extracted with a suitable water immiscible solvent, the solvent layer separated and the product recovered by evaporation of the solvent. The product is obtained typically as an oily liquid which rapidly crystallises, and which can be identified as the desired 2-mercaptothiazole by reference to its NMR spectrum.

It is a feature of the improved process of the invention that the yields of 2-mercaptothiazole which can be obtained are substantially in excess of the 50% reported for the prior art process, and under the most favourable conditions, greater than 70%. It is afurther feature of the invention process that the process does not lead to the concommitant production of the gummy by-products of the prior art process.

Further details of the various aspects of the invention process can be ascertained from the Examples set out below. Examples 1 to 3 describes the production of soluble salts of dithiocarbamic acid and the remaining Examples describe the preparation of 2-mercaptothiazole.

EXAMPLE 1

This Example illustrates the preparation of ammonium dithiocarbamate.

A 500ml 3-necked round bottomed flask was equipped with a gas dispersion tube, thermometer, connection to a hydrogen chloride scrubber unit and magnetic stirring bar. Carbon disulphide (17.5g) and tetrahydrofuran (250ml) were charged to the flask and the stirred contents cooled to 5-10°C. Ammonia (10.5g) was bubbled into the reaction mixture at 5-10°C over the course of 1.5 hours. After this time ammonia was seen to be bubbling through the scrubber solution indicating the end of the reaction. During the course of the reaction a yellow solid formed in the reaction flask. The reaction mixture was allowed to warm to room temperature over 30 minutes, the solid collected by filtration and washed with diethyl ether (2x150ml). The yellow solid was placed in a Buchi flask and dried on a rotary evaporator at 40degC to give the product ammonium dithiocarbamate (23.62g, 93.3% yield) as a well formed pale yellow solid. This material was used without further purification.

^{1}H nmr (DMSO-d_6): 7.7 (br s, NH_2), 7.2 (br s, NH_4)

^{13}C nmr (DMSO-d_6): 217 (s).

EXAMPLE 2

This Example illustrates the preparation of ethyldiisopropylammonium dithiocarbamate.

Anhydrous ammonia (ca. 14.0g) was introduced into a stitted mixture of carbon disulfide (18.8g), isopropyl acetate and ethyldiisopropylamine (48.4g) over a period of 120 minutes whilst maintaining the temperature at 25°C, after which the mixture was sparged

with nitrogen for 30 minutes and the precipitated solid collected by filtration and air dried to yield ethyl diisopropylammonium dithiocarbamate (28.8g).

EXAMPLE 3

This Example illustrates the conversion of ethyldiisopropylammonium dithiocarbamate to sodium dithiocarbamate and the recovery of ethyldiisopropylamine.

An aqueous solution of sodium hydroxide (4.0g) was added dropwise to a stirred solution of ethyldiisopropylammonium dithiocarbamate (22.2g) in water (50 ml) over a period of 30 minutes whilst maintaining the temperature within the range 15 to 20°C , after which the mixture was stirred for a further 30 minutes. The upper layer was collected and identified as ethyldiisopropylamine (10.3g) whilst the lower layer comprised an aqueous solution of sodium dithiocarbamate.

EXAMPLE 4

A 100ml 3-necked round bottomed flask was equipped with a thermometer, condenser, pressure equalising dropping funnel and magnetic stirring bar. Ammonium dithiocarbamate (4.0g) and ethanol (12ml) were charged to the flask and the apparatus flushed with nitrogen. Chloroacetaldehyde (5.7g of a 50wt% aqueous solution) was added dropwise over 30 minutes to the stirred suspension of ammonium dithiocarbamate in ethanol. An exotherm to 38°C was noted during the addition. After the addition of chloroacetaldehyde was complete the reaction mixture was heated at 60°C for 20 hours. It was noted that no gum-like material was formed in the reaction mixture; a gum/resin phase is formed when the reaction is performed using water as the solvent. The mixture was allowed to cool to room temperature, and filtered to remove ammonium chloride. The filtrate was evaporated to remove ethanol and the residual oil/gum partitioned between water (50ml) and ethyl acetate (50ml). The aqueous phase was extracted with additional ethyl acetate (2x50ml). The combined organic phases were dried over anhydrous magnesium sulphate and concentrated by rotary evaporation to give a pale yellow oil which solidified rapidly on standing. This was the product 2-mercaptothiazole (2.739g, 64.4% yield and 89% pure as measured by HPLC analysis. The equivalent yield for 100% strength 2-mercaptothiazole is 57%).

^{1}H nmr (DMSO-d_6): 13.21 (br s, 1H, ArSH), 7.27 (d, J5.5, 1H, ArH), 6.96 (d, J5.5, IH, ArH).
^{13}C nmr (DMSO-d_6): 188.65 (s), 129.18 (s), 114.915 (s)

EXAMPLE 5

A 100ml 3-necked round bottomed flask was equipped with a thermometer, condenser, pressure equalising dropping funnel and magnetic stirring bar. Ammonium dithiocarbamate (4.0g) and ethanol (12ml) were charged to the flask and the apparatus flushed with nitrogen, and the stirred suspension cooled to 0°C (-ice bath cooling). Chloroacetaldehyde (5.7g of a 50wt% aqueous solution) was added dropwise over 30 minutes to the stirred suspension of ammonium dithiocarbamate in ethanol whilst maintaining the reaction temperature at 0°C. It was noted that the reaction mass changes colour from yellow to light grey/white during the addition. Once addition of the chloroacetaldehyde was complete the reaction was stirred at 0°C for a further 30 minutes. The reaction mixture was then warmed to 60°C and stirred and heated at this temperature for 16 hours. It was noted that no gum-like material was formed in the reaction mixture; a gum/resin phase is formed when the reaction is performed using water as the solvent. The mixture was allowed to cool to room temperature, filtered to remove ammonium chloride. The filtrate was evaporated to remove ethanol and the residual oil/gum partitioned between water (50ml) and ethyl acetate (50ml). The aqueous phase was extracted with additional ethyl acetate (2x50ml). The combined organic phases were dried over anhydrous magnesium sulphate and concentrated by rotary evaporation to give a pale yellow oil which solidified rapidly on standing. This was the product 2-mercaptothiazole (2.981g, 73.9% yield and 93.9% pure as measured by HPLC analysis. The equivalent yield for 100% strength 2-mercaptothiazole is 68.8%).

^{1}H nmr (DMSO-d_6): 13.21 (br s, 1H, ArSH), 7.27 (d, J5.5, 1H, ArH), 6.96 (d, J5.5, IH, ArH).

^{13}C nmr (DMSO-d_6): 188.65 (s), 129.18 (s), 114.915 (s)

EXAMPLE 6

A 100ml 3-necked round bottomed flask was equipped with a thermometer, condenser, pressure equalising dropping funnel and magnetic stirring bar. Ammonium dithiocarbamate (4.0g) and tert-butanol (24ml) were charged to the flask and the apparatus flushed with nitrogen, and the stirred suspension cooled to 5°C (-ice bath cooling). Chloroacetaldehyde (5.7g of a 50wt% aqueous solution) was added dropwise over 30 minutes to the stirred suspension of ammonium dithiocarbamate in tert-butanol whilst maintaining the reaction temperature at 5°C. Two liquid phases were observed after the

addition of chloroacetaldehyde was complete. The reaction was stirred at 0°C for a further 30 minutes and then warmed to 60°C and stirred and heated at this temperature for 18 hours. It was noted that no gum-like material was formed in the reaction mixture. The mixture was allowed to cool to room temperature, filtered to remove ammonium chloride. The filtrate was evaporated to remove tert-butanol and the residue partitioned between water (50ml) and ethyl acetate (50ml). The aqueous phase was extracted with additional ethyl acetate (2x50ml). The combined organic phases were dried over anhydrous magnesium sulphate and concentrated by rotary evaporation to give a pale yellow oil which solidified rapidly on standing. This was the product 2-mercaptothiazole (2.874g, 67.6% yield and 88.4% pure as measured by HPLC analysis. The equivalent yield for 100% strength 2-mercaptothiazole is 59.8%).

^{1}H nmr (DMSO-d_6): 13.21 (br s, 1H, ArSH), 7.27 (d, J5.5, 1H, ArH), 6.96 (d, J5.5, IH, ArH).

^{13}C nmr (DMSO-d_6): 188.65 (s), 129.18 (s), 114.915 (s)

EXAMPLE 7

A 100ml 3-necked round bottomed flask was equipped with a thermometer, condenser, nitrogen inlet, septum, and magnetic stirring bar. Ammonium dithiocarbamate (3.943g) and normal-propanol (24ml) were charged to the flask, stirring commenced and the apparatus flushed with nitrogen and cooled to 0°C. Chloroacetaldehyde (5.574g of a 50wt% aqueous solution) was added to the stirred slurry over 45 minutes using a syringe pump. The reaction was stirred at 0°C for a further 1 hour and then warmed to 60°C and stirred and heated at this temperature for 7 hours. It was noted that no gum-like material was formed in the reaction mixture, and the reaction mixture becomes pale yellow coloured on heating. The mixture was allowed to cool to room temperature and evaporated to remove normal-propanol and water. The residue was partitioned between water (15ml) and ethyl acetate (25ml). The aqueous phase was extracted with additional ethyl acetate (20ml). The combined organic phases were dried over anhydrous magnesium sulphate and concentrated by rotary evaporation to give a pale yellow oil which solidified rapidly on standing. This was the product 2-mercaptothiazole (3.344g, 80.5% yield and 92.4% pure as measured by HPLC analysis. The equivalent yield for 100% strength 2-mercaptothiazole is 74.4%).

^{1}H nmr (DMSO-d_6): 13.21 (br s, 1H, ArSH), 7.27 (d, J5.5, 1H, ArH), 6.96 (d, J5.5, IH, ArH).

^{13}C nmr (DMSO-d_6): 188.65 (s), 129.18 (s), 114.915 (s)

EXAMPLE 8

A 50ml 3-necked round bottomed flask was equipped with a thermometer, condenser, nitrogen inlet, and magnetic stirring bar. Ammonium dithiocarbamate (7.993g) and ethanol (11ml) were charged to the flask, stirring commenced and the apparatus flushed with nitrogen and cooled to 0°C. Chloroacetaldehyde (10.828g of a 50wt% aqueous solution) was added to the stirred slurry over 1 hour using a syringe pump. During this time, the formation of white ammonium chloride was noted. After the addition was complete the reaction mixture was stirred at 0°C for a further 45 minutes prior to heating heated at 60°C for 16 hours. After this time, it was noted that a small glassy bead of solid material had formed in the reaction mixture; this solid bead was mobile and did not adhere to any parts of the reaction apparatus. No gum-like material was formed in the reaction mixture; a gum/resin phase is formed when the reaction is performed using water as the solvent. The mixture was allowed to cool to room temperature, and decanted from the small glass-like bead. The bead weighed 0.445g. The remaining mixture was evaporated to remove ethanol and water and the residue partitioned between water (20ml) and ethyl acetate (25ml). The aqueous phase was extracted with additional ethyl acetate (25ml). The combined organic phases were dried over anhydrous magnesium sulphate and concentrated by rotary evaporation to give a pale yellow solid. This was the product 2-mercaptothiazole (6.331g, 78.5% yield and 93.2% pure as measured by HPLC analysis. The equivalent yield for 100% strength 2-mercaptothiazole is 73.1%).

^{1}H nmr (DMSO-d_6): 13.21 (br s, 1H, ArSH), 7.27 (d, J5.5, 1H, ArH), 6.96 (d, J5.5, IH, ArH).

^{13}C nmr (DMSO-d_6): 188.65 (s), 129.18 (s), 114.915 (s)

EXAMPLE 9

A 100ml 3-necked round bottomed flask was equipped with a thermometer, condenser, pressure equalising addition funnel, nitrogen inlet, and magnetic stirring bar. Ammonium dithiocarbamate (7.860g) and ethanol (24ml) were charged to the flask, stirring commenced and the apparatus flushed with nitrogen and cooled to 0°C. Chloroacetaldehyde (11.194g of a 50wt% aqueous solution) was added dropwise to the stirred slurry over 0.75 hour. During this time, the formation of white ammonium chloride was noted. After the addition was complete the reaction mixture was stirred at 0°C for a further 40 minutes, and then allowed to warm to room temperature over 20 minutes. The mixture was then heated to

60°C over 0.5 hours; when the reaction temperature had reached 40°C concentrated hydrochloric acid (0.75ml) was added to the adjust the reaction mixture to pH2. After 1 hour heating at 60°C, HPLC analysis of the pale brown mixture indicated that the reaction was complete. No gum-like material was formed in the reaction mixture; a gum/resin phase is formed when the reaction is performed using water as the solvent. The mixture was allowed to cool to room temperature. The mixture was evaporated to remove ethanol and water and the residue partitioned between water (30ml) and ethyl acetate (50ml). The aqueous phase was extracted with additional ethyl acetate (2x50ml). A very small amount of insoluble brown solid remained in the aqueous phase. The combined organic phases were dried over anhydrous magnesium sulphate and concentrated by rotary evaporation to give a pale brown solid. This was the product 2-mercaptothiazole (6.663g, 79.8% yield and 88.5% pure as measured by HPLC analysis. The equivalent yield for 100% strength 2-mercaptothiazole is 70.7%).

^{1}H nmr (DMSO-d_6): 13.21 (br s, 1H, ArSH), 7.27 (d, J5.5, 1H, ArH), 6.96 (d, J5.5, IH, ArH).

^{13}C nmr (DMSO-d_6): 188.65 (s), 129.18 (s), 114.915 (s)

EXAMPLE 10

A 100ml 3-necked round bottomed flask was equipped with a thermometer, condenser (with nitrogen inlet), and magnetic stirring bar. Two ports were fitted with rubber septa. Ethanol (30ml) was charged to the flask, stirring commenced and the apparatus flushed with nitrogen and cooled to 0°C. Ammonium dithiocarbamate (5.087g) in water (8ml) and chloroacetaldehyde (5.7g of a 50wt% aqueous solution) were added dropwise over 40 minutes to the ethanol. Syringes operated by syringe pumps were employed for the controlled addition; the syringe containing the ammonium dithiocarbamate solution was allowed to introduce material to the flask for two minutes prior to starting the delivery of the chloroacetaldehyde reagent. No solid precipitates were observed during the course of the reaction. After the addition of the reagents was complete the slightly turbid reaction mixture was stirred at 0°C for a further 40 minutes prior to allowing to warm to room temperature over 20 minutes. The reaction mixture was then warmed to 60°C; when the reaction temperature had reached 40°C concentrated hydrochloric acid (0.75ml) was added to the adjust the reaction mixture to pH2. The reaction mixture turned pale yellow over approximately 10 minutes. After 20 minutes heating at 60°C HPLC analysis of the mixture

indicated that the reaction was complete. It was noted that no gum-like material was formed in the reaction mixture; a gum/resin phase is formed when the reaction is performed using water as the solvent. The mixture was allowed to cool to room temperature, and evaporated to remove ethanol and water and the residue partitioned between water (20ml) and ethyl acetate (30ml). The aqueous phase was extracted with additional ethyl acetate (2x30ml). The combined organic phases were dried over anhydrous magnesium sulphate and concentrated by rotary evaporation to give a pale yellow oil which solidified rapidly on standing to leave a light tan solid. This was the product 2-mercaptothiazole (4.417g, 81.8% yield and 94.5% pure as measured by HPLC analysis. The equivalent yield for 100% strength 2-mercaptothiazole is 77.3%).

^{1}H nmr ($CDCl_3$) : 12.50(br s, 1H, ArSH), 7.05(d, J5.5, 1H, ArH), 6.71(d,J5.5, 1H, ArH).
^{13}C nmr ($CDCl_3$): 188.5 (s), 128 (s), 115 (s).

EXAMPLE 11

A 100ml 3-necked round bottomed flask was equipped with a thermometer, condenser, and magnetic stirring bar. Two ports were fitted with rubber septa. Ethanol (24ml) was charged to the flask, stirring commenced and the apparatus flushed with nitrogen and cooled to 0°C. Ammonium dithiocarbamate (4.0g) in water (15ml) and Chloroacetaldehyde (5.7g of a 50wt% aqueous solution) were added dropwise over 45 minutes to the ethanol. Syringes operated by syringe pumps were employed for the controlled addition; the syringe containing the ammonium dithiocarbamate solution was allowed to introduce material to the flask for five minutes prior to starting the delivery of the chloroacetaldehyde reagent. No solid precipitates were observed during the course of the reaction After the addition of the reagents was complete the slightly turbid reaction mixture was stirred at 0°C for a further 30 minutes prior to heating heated at 60°C for 6 hours. The reaction mixture turned pale yellow upon heating. It was noted that no gum-like material was formed in the reaction mixture; a gum/resin phase is formed when the reaction is performed using water as the solvent. The mixture was allowed to cool to room temperature, and filtered to remove ammonium chloride. The filtrate was evaporated to remove ethanol and water and the residue partitioned between water (50ml) and ethyl acetate (50ml). The

aqueous phase was extracted with additional ethyl acetate (2x50ml). The combined organic phases were dried over anhydrous magnesium sulphate and concentrated by rotary evaporation to give a pale yellow oil which solidified rapidly on standing. This was the product 2-mercaptothiazole (3.267g, 76.9% yield and 93.8% pure as measured by HPLC analysis. The equivalent yield for 100% strength 2-mercaptothiazole is 72.1%).

^{1}H nmr (DMSO-d_6): 13.21 (br s, 1H, ArSH), 7.27 (d, J5.5, 1H, ArH), 6.96 (d, J5.5, IH, ArH).

^{13}C nmr (DMSO-d_6): 188.65 (s), 129.18 (s), 114.915 (s)

CLAIMS

1. A process for preparing 2-mercaptothiazole by reacting a water soluble salt of dithiocarbamic acid with 2-haloacetaldehyde characterised in that the 2-haloacetaldehyde is added to a slurry of the salt of dithiocarbamic acid in solid form in a water-miscible diluent in which the salt is substantially insoluble.

2. A process according to claim 1 in which the slurry is maintained at a temperature within the range -10°C to +15°C during the addition.

3. A process according to claim 1 or claim 2 in which the 2-haloacetaldehyde is added in the form of an aqueous solution.

4. A process according to any of claims 1 to 3 in which the resultant reaction mixture is heated at a temperature within the range from about 50°C to the reflux temperature to complete the reaction.

5. A process according to claim 4 in which the pH of the reaction mixture is adjusted to a value within the range 1 to 3.

6. A process according to claim 1 in which the diluent is a C_{1-4} alkanol.

7. A process according to claim 1 in which the salt is an alkali metal or ammonium salt.

8. A process according to claim 1 or claim 3 in which the 2-haloacetaldehyde is 2-chloroacetaldehyde or the hydrate thereof.

9. A process according to claim 1 wherein an aqueous solution of 2-chloroacetaldehyde is added to a slurry of ammonium dithiocarbamate in a C_{1-4} alkanol at a temperature within the range -10°C to +15°C, and the resultant reaction mixture heated at a temperature within the range from about 50°C to the reflux temperature to complete the reaction.

10. A process according to claim 9 wherein the pH of the reaction mixture is adjusted to a value within the range 1 to 3 after the addition of the 2-chloroacetaldehyde.

11. A process for preparing 2-mercaptothiazole by reacting a water soluble salt of dithiocarbamic acid with 2-haloacetaldehyde characterised in that the 2-haloacetaldehyde and a solution of the the salt of dithiocarbamic acid are separately and simultaneously delivered at substantially equimolar rates of addition to a reaction vessel containing a water-miscible diluent in which the salt is substantially insoluble.

12. A process according to claim 11 wherein the diluent contains a minor amount of the salt of dithiocarbamic acid prior to the addition of the 2-haloacetaldehyde.

13. A process according to claim 11 wherein an aqueous solution of 2-chloroacetaldehyde and an aqueous solution of ammonium dithiocarbamate acid are separately and simultaneously delivered at substantially equimolar rates of addition to a reaction vessel containing in a C_{1-4} alkanol at a temperature within the range -10°C to +15°C, and the resultant reaction mixture heated at a temperature within the range from about 50°C to the reflux temperature to complete the reaction.

14. A process according to claim 13 wherein the pH of the reaction mixture is adjusted to a value within the range 1 to 3 after the addition of the 2-chloroacetaldehyde and the ammonium dithiocarbamate.

15. A process for preparing a tertiary ammonium salt of a dithiocarbamic acid which comprises reacting ammonia with carbon disulfide in the presence of a molar or excess quantity with respect to carbon disulfide of a tertiary amine having a pK_b greater than that of ammonia under the reaction conditions in the presence of a non-aqueous liquid diluent in which the tertiary ammonium salt of dithiocarbamic acid is substantially insoluble.

16. A process for preparing an aqueous solution of an alkali metal salt of dithiocarbamic

acid which comprises treating an aqueous solution of a tertiary ammmonium salt of dithiocarbamic acid with an alkali metal hydroxide.

17. The process according to claim16 where the tertiary ammonium salt of dithiocarbamic acid is prepared by the process of claim 15.

18. The process of claim 17 where the teriary amine is recovered from the reaction mixture and recycled for use in the process of claim 15.

19. The process of claim 15 where the tertiary amine is a trialkylamine having at least 8 carbon atoms.

20. The process of claim 19 wherein the tertiary amine is ethyldiisopropylamine.

21. A tertiary ammonium salt of dithiocarbamic acid derived from a trialkylamine having at least 8 carbon atoms.

22. Ethyldiisopropylammonium dithiocarbamate.

The Patent Office

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Application No:	GB 9803430.9	**Examiner:**	S.I.Ahmad
Claims searched:	1-14	**Date of search:**	22 April 1998

Patents Act 1977
Search Report under Section 17

Databases searched:

UK Patent Office collections, including GB, EP, WO & US patent specifications, in:

UK Cl (Ed.P): C2C(CQM,CGC)

Int Cl (Ed.6): C07D-277/36

Other: Data-base : Cas-on-line

Documents considered to be relevant:

Category	Identity of document and relevant passage	Relevant to claims
	No relevant document	

X	Document indicating lack of novelty or inventive step	A	Document indicating technological background and/or state of the art.
Y	Document indicating lack of inventive step if combined with one or more other documents of same category.	P	Document published on or after the declared priority date but before the filing date of this invention.
&	Member of the same patent family	E	Patent document published on or after, but with priority date earlier than, the filing date of this application.